

Case Report

Idiopathic Premature Ventricular Contraction Originating from Left Epicardial Outflow Tract —Effects of Antiarrhythmic Drugs, Autonomic Provocation and Radiofrequency Catheter Ablation—

Kotaro Miyaji MD^{*1}, Mitsuhiro Nishizaki MD^{*1}, Toru Ogawa MD^{*1}, Shinji Sugawara MD^{*1}, Hiroyuki Fujii MD^{*1}, Takashi Ashikaga MD^{*1}, Noriyoshi Yamawake MD^{*1}, Harumizu Sakurada MD^{*2}, Masayasu Hiraoka MD FACC^{*3}

^{*1}Department of Cardiology, Yokohama Minami Kyosai Hospital

^{*2}Department of Cardiology, Tokyo Metropolitan Hiroo Hospital

^{*3}Department of Cardiovascular Diseases, Medical Research Institute, Tokyo Medical and Dental University

We present a patient with frequent episodes of palpitation who had idiopathic premature ventricular contraction (PVC) with QRS morphology exhibiting a right bundle branch block pattern with an inferior axis. Neither administration of procainamide, propranolol, lidocaine or verapamil could inhibit PVC, whereas administration of adenosine triphosphate, carotid sinus massage and Valsalva maneuver could effectively eliminate PVC. The earliest activation preceding the QRS complex by 25 msec at occurrence of the PVC was recorded at the distal site of the coronary sinus and within the left coronary cusp. Pacemapping in the supraventricular site during sinus rhythm produced a QRS complex more similar to PVC than that produced in the infraventricular site of the left ventricular outflow tract (LVOT). Radiofrequency catheter ablation was performed at the supraventricular site close to the epicardial LVOT, which resulted in successful elimination of PVCs.
(J Arrhythmia 2006; 22: 58–65)

Key words: Idiopathic premature ventricular contraction, Left ventricular outflow tract, Ablation, Triggered activity

Introduction

Although premature ventricular contractions (PVCs) and ventricular tachycardia (VT) in the structurally normal heart are not always associated with life-threatening consequences,¹⁾ they are some-

times refractory to antiarrhythmic agents and their symptoms are often severe. There have been some reports of catheter ablation of PVCs and VT originating from the left ventricular outflow tract (LVOT), in which the success rate of catheter ablation was high and this method of treatment

Received 29, June, 2005; accepted in final form 8, February, 2006.

Address for correspondence: Mitsuhiro Nishizaki MD, Department of Cardiology, Yokohama Minami Kyosai Hospital, 1-21-1 Mitsuura-Higashi, Kanazawaku, Yokohama, Kanagawa 236-0037, Japan. Fax: 81-45-701-9159 Tel: 81-45-782-2101

E-mail: kotaro@wa2.so-net.ne.jp

was thought to be effective for eliminating these arrhythmias.²⁾ However, there has not been an exploration of the effects of pharmacological intervention, autonomic provocation and radiofrequency catheter ablation on PVC originating from LVOT. In this article, we report a case with idiopathic PVC originating from LVOT, which was terminated by administration of adenosine triphosphate (ATP) together with vagal stimulation and abolished by radiofrequency energy applied at the supra-ventricular region of the left coronary cusp.

Case Report

A 40-year-old male with a history of symptomatic PVC refractory to medical therapy was referred to our hospital for radiofrequency catheter ablation. The QRS morphology of the PVC was right bundle branch block and inferior axis pattern. He had experienced episodes of palpitation during exertion for the last six months. Routine examinations including echocardiography, left ventriculography and coronary angiography revealed no apparent structural heart disease. However, for the last three months, he had more frequent episodes of palpitation than before, and the 24 hours Holter ECG detected frequent episode of PVCs (i.e., 35679 beats per day). The PVC was refractory to administration of several antiarrhythmic agents of class I and amiodarone. The cardiac size was getting larger as seen by chest X-P with cardiothoracic ratio of 48% to 52%, and the BNP value also increased. Echocardiography demonstrated dilatation of left ventricular space with

diastolic diameter of 58 mm and mild reduction of ejection fraction to 54%.

Surface ECG revealed frequent PVC with QRS complex of right bundle branch block and inferior axis with a dominant R wave in all precordial leads (Figure 1).

We elucidated effects of antiarrhythmic agents and vagal stimulation on the PVC. Right carotid sinus massage (CSM) eliminated the PVC, and left CSM and Valsalva maneuver diminished the frequency of the PVC (Figure 2A). Intravenous injections of several antiarrhythmic drugs, including procainamide, propranolol, lidocaine and verapamil were not effective for elimination of PVC (Figure 2B), however, bolus injection of ATP with 10 mg inhibited PVC distinctively (Figure 2C).

After informed consent was obtained, electrophysiological study and catheter ablation were performed in a drug-free state. Electrode catheters were positioned in right ventricular apex, right ventricular outflow tract, coronary sinus and septal site of high right atrium (Figure 3A). The earliest activation was obtained at the distal site of the coronary sinus (CS1–2) during development of the PVC, and that preceded the QRS complex by 25 msec. A mapping study was attempted with an electrode catheter located in the left ventricle. The earliest activation during development of the PVC was recorded at the infravalvular region of the LVOT, which preceded the QRS complex by 15 msec (ABL1–2 in Figure 3B). Pacemapping at this site during sinus rhythm produced a QRS

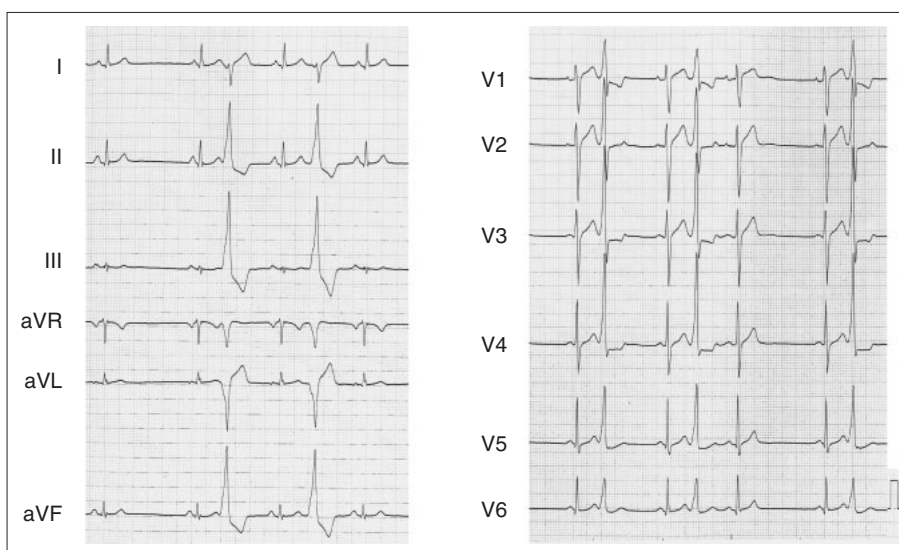


Figure 1 Surface twelve-lead ECG during occurrence of PVCs. The morphology of the QRS complex of PVC exhibited right bundle branch block pattern with inferior axis.

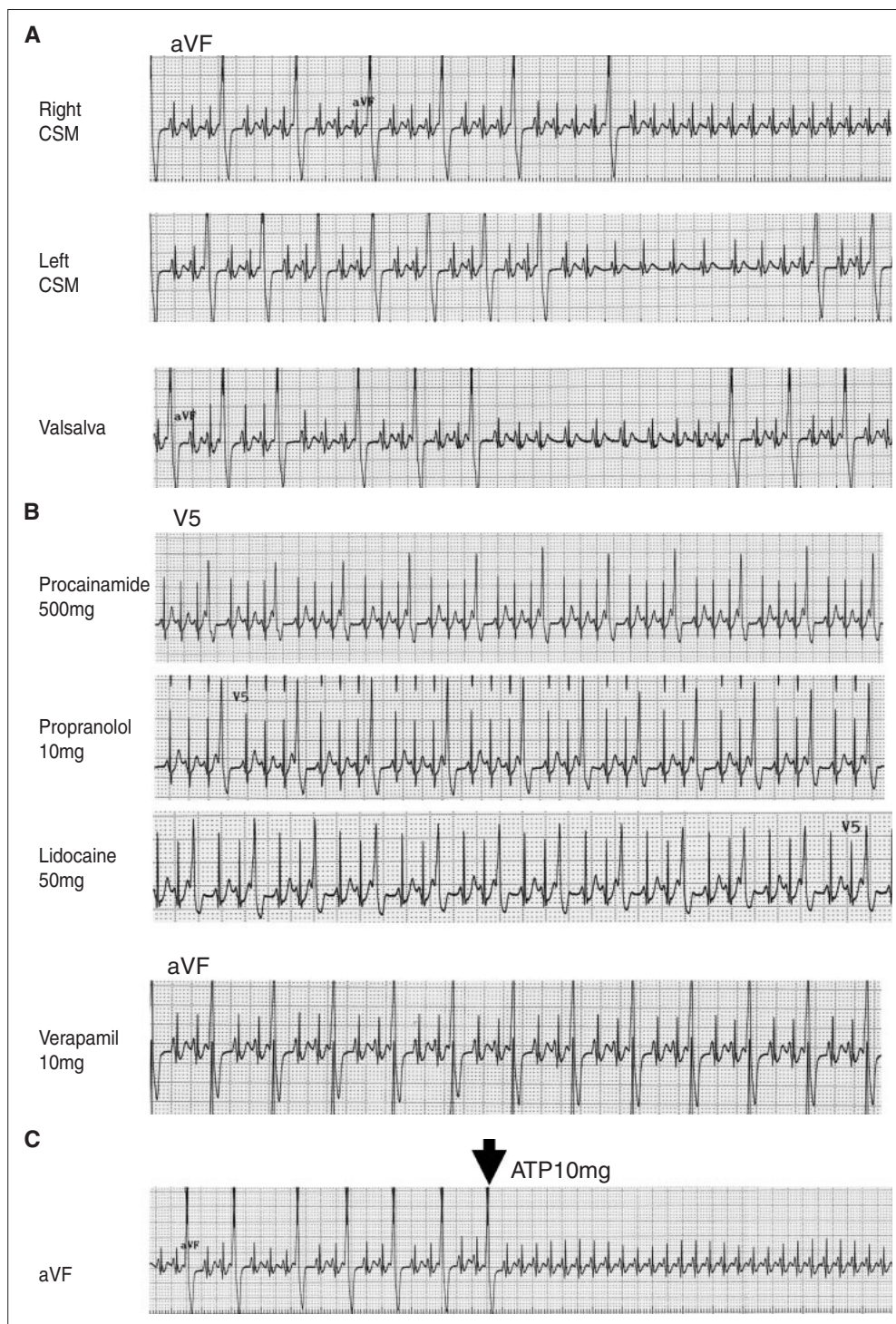


Figure 2

A: ECG during carotid sinus massage (CSM) and Valsalva maneuver during development of PVC. Right CSM distinctively inhibited PVC and left CSM and Valsalva maneuver diminished PVC.

B: ECG during administration of several antiarrhythmic drugs for PVC. Neither procainamide, propranolol, lidocaine nor verapamil could inhibit PVCs.

C: Limb lead of ECG after administration of adenosine triphosphate during occurrence of PVC. PVCs were eliminated immediately after bolus injection of ATP. ATP, adenosine triphosphate.

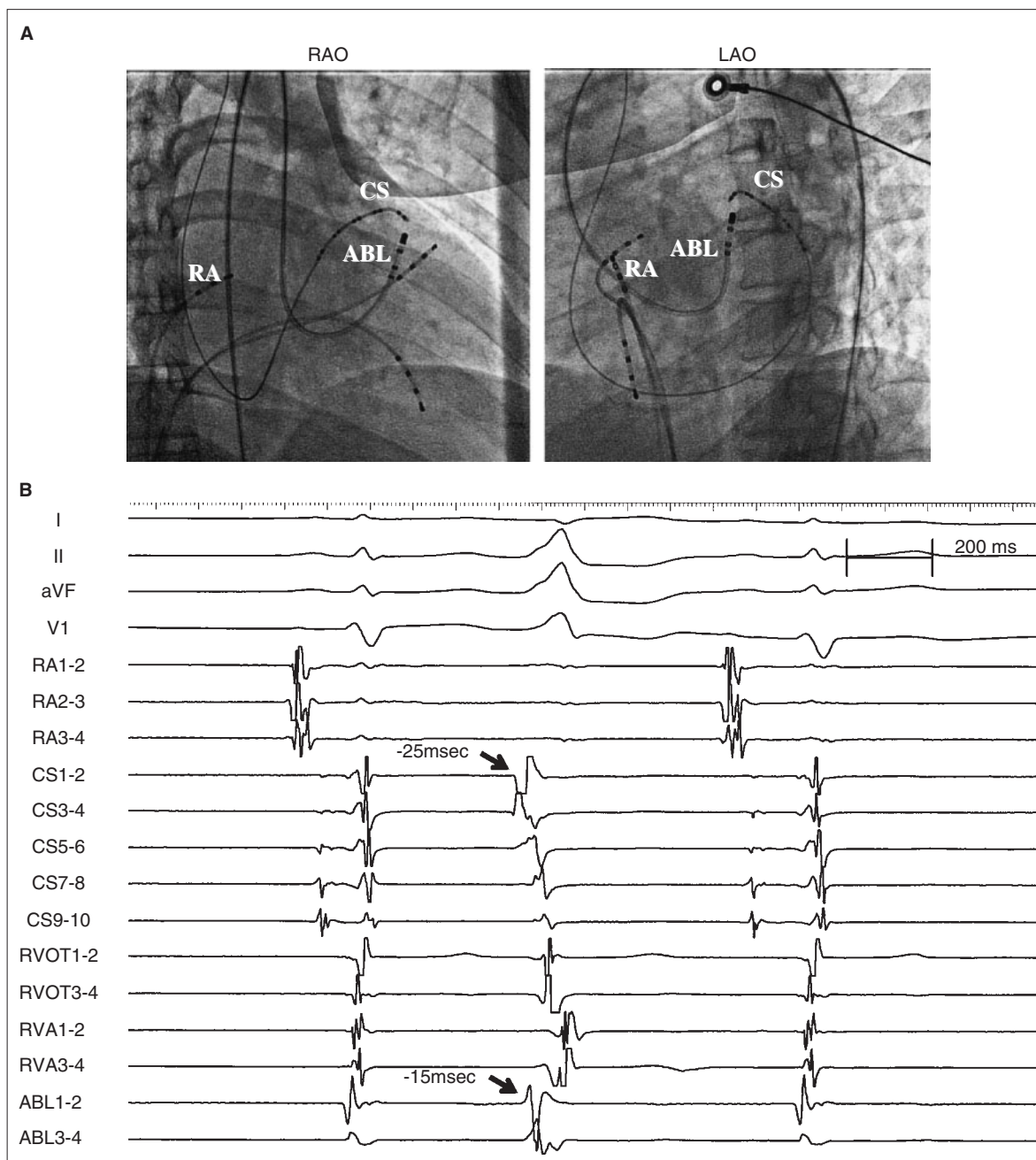


Figure 3

A: Fluoroscopic images during endocardial mapping at the infravalvular left ventricular site. RAO, right anterior oblique view; LAO, left anterior oblique view; CS, coronary sinus; ABL, ablation catheter.

The distal electrode pair of the ablation catheter was located in the infravalvular region of the left ventricular outflow tract close to the distal electrode pair of the CS (CS 1,2).

B: Intracardiac electrograms during sinus rhythm and appearance of PVC (The infravalvular site). RA, septal site of high right atrium; CS, coronary sinus; RVOT, right ventricular outflow tract; RVA, right ventricular apex; ABL, ablation catheter.

The local ventricular potentials at the distal site of coronary sinus (CS1-2) and at the distal electrode pair of ablation catheter in the infravalvular left ventricular outflow tract preceded the QRS complex by 25 msec and 15 msec, respectively.

complex similar to that of the PVC in a surface 12-lead ECG, although the QRS width was slightly narrower than that of the PVC (Figure 4). Activation

mapping system (CARTO, Biosense Webster, Inc) (Figure 5) showed the LVOT site to be located at the anterior left ventricular wall below the aortic valve.

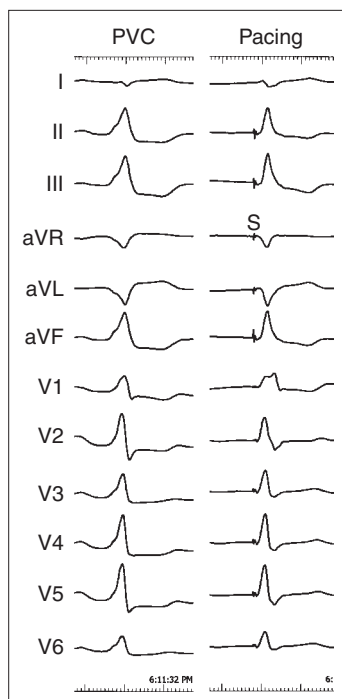


Figure 4 Comparison between the QRS complex at PVC and at pacemapping in the infravalvular region. S indicates a stimulation artifact.

Pacing at the infravalvular site of the left ventricular outflow tract during sinus rhythm produced a similar but slightly narrower QRS complex as compared with that of the PVC.

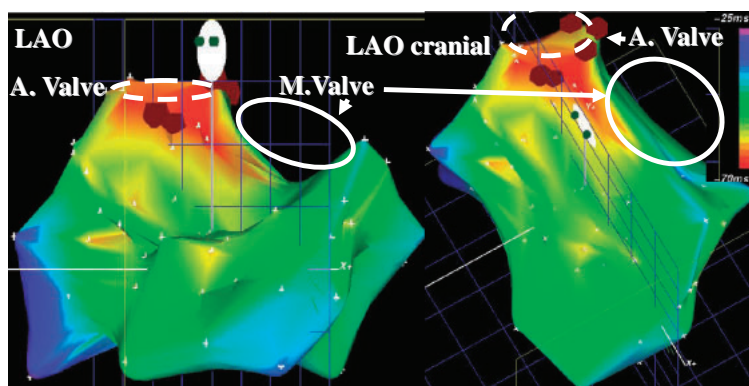


Figure 5 CARTO images of activation mapping during PVC appearance. LAO, left anterior oblique view; A. valve, aortic valve; M. valve, mitral valve. The earliest activation site (red zone) was recorded at anterior wall of left ventricle below the aortic valve.

Radiofrequency catheter ablation was performed at this endocardial site, but PVC was not inhibited.

We investigated the local electrograms close to coronary cusps above the aortic valve. The slight insertion of the electrode catheter into the CS could result in the shift of the earliest activation from CS 1–2 to CS 5–6 during development of the PVC. The earliest activation was obtained at the distal electrode pair close to the left coronary cusp during

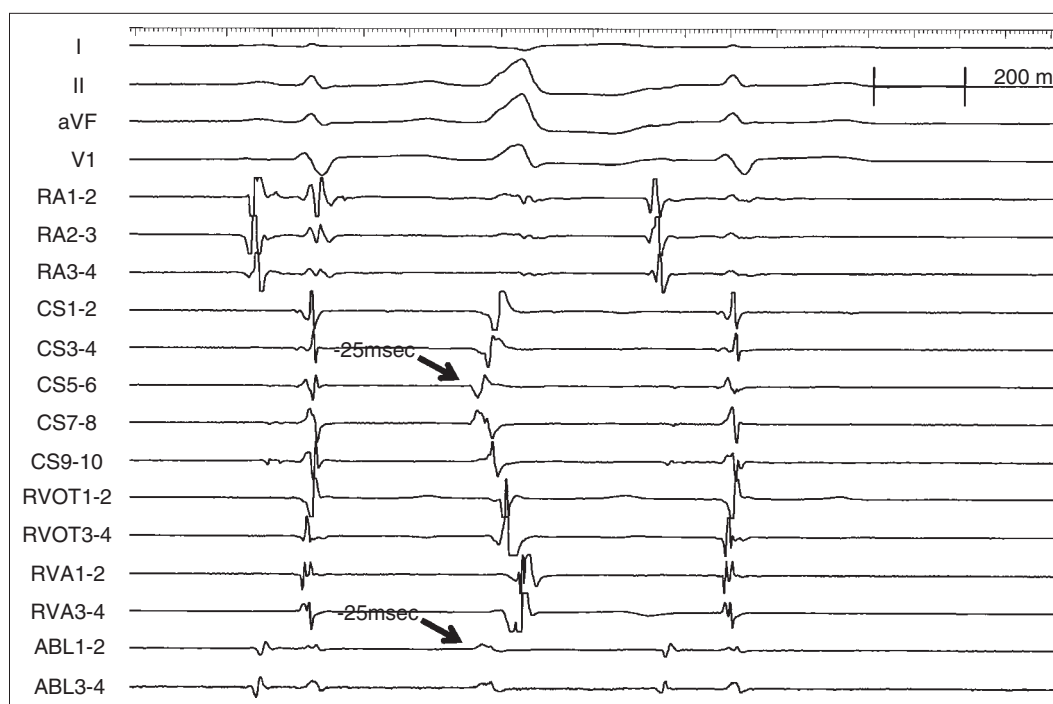


Figure 6 Intracardiac electrograms during appearance of PVC (the supraventricular site). Both the ventricular potentials recorded at the distal site of coronary sinus (CS5–6) and at the distal electrode pair of ablation catheter in the supraventricular left ventricular outflow tract preceded the QRS complex by 25 msec.

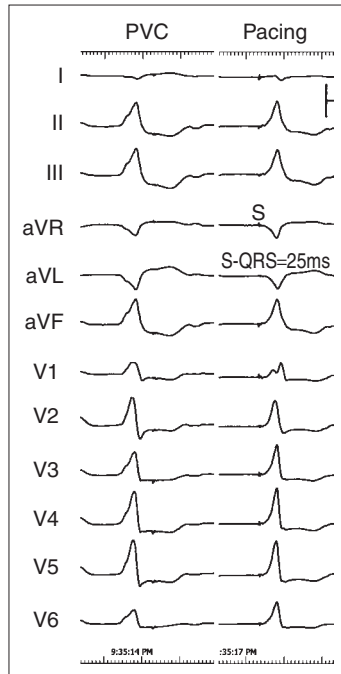


Figure 7 Comparison between the QRS complex at PVC and at pacemapping in the supra-ventricular region. S indicates a stimulation artifact.

Pacemapping at the supra-ventricular site of LVOT during sinus rhythm exhibited the QRS complex more similar to that of the PVC than that done at the infra-ventricular site.

development of the PVC and which preceded the QRS complex by 25 msec, in which the local electrogram was recorded concurrently with those of the CS 5–6 electrode (**Figure 6**). Pacemapping at this site during sinus rhythm exhibited a QRS complex more similar to the PVC's compared with that at the infra-ventricular site of LVOT (**Figure 7**). Radiofrequency energy was delivered in this site (**Figure 8**) during development of the PVC at a power of 30 to 50 W with a target temperature of 60°C, resulting in elimination of PVC at 10 seconds after the commencement of application (**Figure 9**).

Discussion

In case of idiopathic VT (or PVC) from the right ventricular outflow tract, the origin is classified precisely by analysis of QRS morphology and body surface maps,³⁾ but in case of VT (PVC) from the LVOT, it is classified more briefly. By analysis of QRS morphology, PVCs with QRS morphology exhibiting right bundle branch block, broad R wave in the precordial leads and inferior axis type originate from various sites of the left ventricular outflow tract, whereas those showing left bundle branch block type, inferior axis and transition zone of V1 or V2 type originate from the basal aspect of

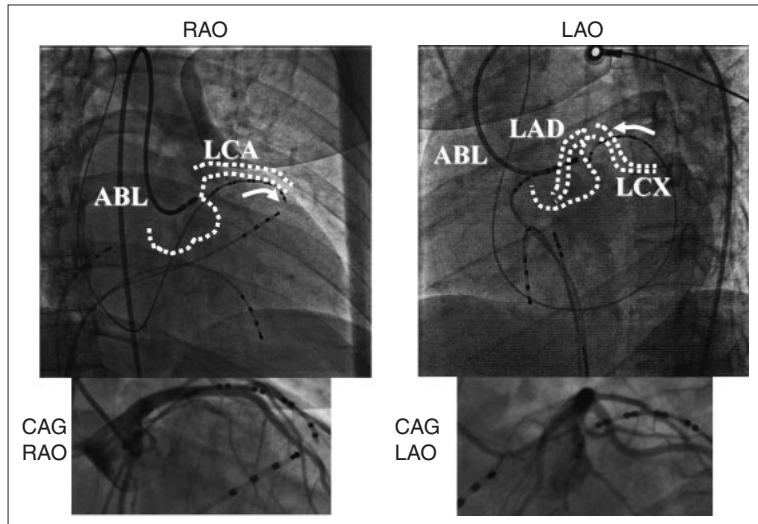


Figure 8 Fluoroscopic images of the relationship between the catheter position of successful ablation and the left coronary artery.

Radiofrequency ablation catheter was located close to the left coronary cusp in the supra-ventricular site. ABL, ablation catheter; LCA, left coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; CAG, coronary angiography.

the superior left ventricular septum.^{4–6)} On the other hand, whether the VT (PVC) originates above or below the aortic valve can also be estimated from the QRS morphology. Hachiya et al.⁷⁾ reported the relationship between the origin of the PVC and ECG findings. They reported that the QRS morphology with S wave in lead I, precordial R wave transition in lead V1 or V2 and no S wave in lead V5 or V6 suggests that the origin of the PVC is localized at the supra-aortic valvular region, whereas S wave in lead I, tall R waves in leads V1 and V2, and S wave observed in lead V5 or V6 suggests that the origin of the PVC is localized at the infra-aortic valvular region. In this case, by the analysis of the QRS configuration of the PVC, its origin was thought to be localized at the supra-aortic valvular region. However, the earliest ventricular activation during development of the PVC was recorded both at the distal pair of the CS electrode and at the site close to coronary cusp in the supra-ventricular region. Therefore, the origin of this PVC was assumed to be located at the epicardium between the aortic valve and the distal portion of the CS. This was proved by the fact that radiofrequency ablation at the site close to the coronary cusp in the supra-ventricular region was more effective for termination of PVC than at the endocardium of the LVOT.

The mechanism of idiopathic VT from right ventricular outflow tract is well recognized to be cyclic adenosine monophosphate (c-AMP)-mediated triggered activity.⁸⁾ Therefore it is assumed to be

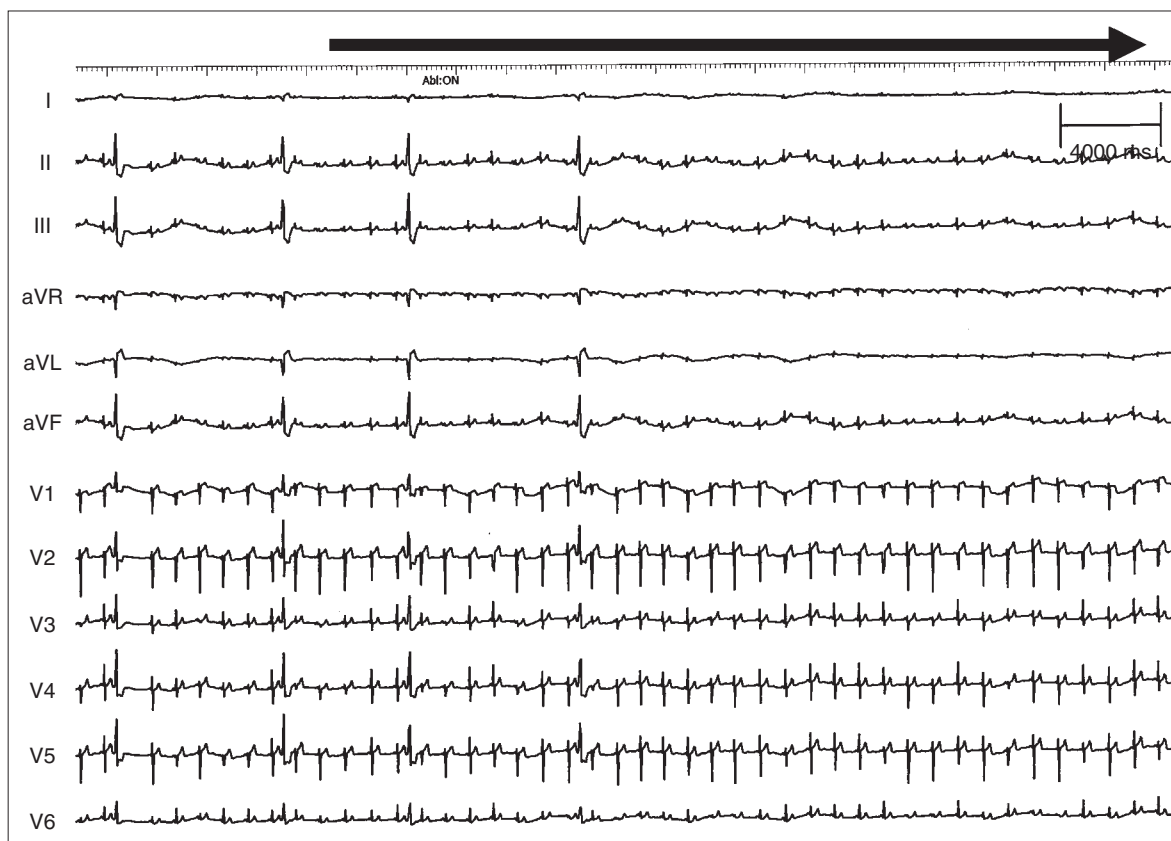


Figure 9 Surface 12-lead ECG during the successful radiofrequency energy application. PVC was successfully inhibited at 10 seconds after the commencement of application.

inhibited by adenosine, vagal maneuvers, β -blockers, and calcium channel blockers. To the contrary, PVC and VT from the left ventricular outflow tract are observed infrequently, and so this mechanism has not been well elucidated. Idiopathic left VTs have been reported to be classified into three categories according to pharmacological effects⁹⁾ as the verapamil sensitive type, the adenosine sensitive type and the automatic (propranolol sensitive) type. The adenosine sensitive type is thought to originate in the interventricular septum and exit to some regions, for example, the LVOT. It results from cAMP-stimulated intracellular calcium overload, and theoretically it is inhibited by Valsalva maneuvers, pharmacological intervention of verapamil, β -blockers and adenosine. However, the response of PVC from the LVOT to these antiarrhythmic drugs remains unclear between supra- and infra-valvular site. It has been reported that responses of PVC from the LVOT to antiarrhythmic drugs were not uniform and especially, the effects of propranolol and verapamil on the PVC were different in individual cases compared with those of the PVC from the right ventricular outflow tract.^{6,10,11)} On the

other hand, both vagal stimulation and ATP produce the same cardiac effect and share a similar receptor-effector coupling system, which activates the inhibitory G_i protein, and decreases the c-AMP due to inhibition of adenylate cyclase.¹²⁾ Therefore, Lerman et al.¹²⁾ emphasized that the mechanism of adenosine-sensitive ventricular tachycardia in which adenosine is effective is due to c-AMP mediated triggered activity, although it has been reported that ATP has c-AMP independent actions associated with decrease of Ca^{2+} influx.^{12,13)}

In this case, vagal stimulation and administration of ATP were distinctively effective for inhibiting the PVC which was not inhibited by antiarrhythmic agents including propranolol and verapamil. Its response to such a pharmacological intervention suggests that the possible mechanism of the PVC from the epicardial site of the LVOT may be triggered activity.

References

- 1) Goy JJ, Tauxe F, Fromer M, Schlapfer J, Vogt P, Kappenberger L: Ten-years follow-up of 20 patients with

- idiopathic ventricular tachycardia. *PACE* 1990; 13: 1142–1147
- 2) Seidl K, Schumacher B, Hauer B, Jung W, Drogemuller A, Senges J, Luderitz B: Radiofrequency catheter ablation of frequent monomorphic ventricular ectopic activity. *J Cardiovasc Electrophysiol* 1999; 10: 924–934
 - 3) Kamakura S, Shimizu W, Matsuo K, Taguchi A, Suyama K, Kurita T, Aihara N, Ohe T, Shimomura K: Localization of optimal ablation site of idiopathic ventricular tachycardia from right and left ventricular outflow tract by body surface ECG. *Circulation* 1998; 98: 1525–1533
 - 4) Shimoike E, Ohnishi Y, Ueda N, Maruyama T, Kaji Y: Radiofrequency catheter ablation of left ventricular outflow tract tachycardia from the coronary cusp: a new approach to the tachycardia focus. *J Cardiovasc Electrophysiol* 1999; 10: 1005–1009
 - 5) Callans DJ, Menz V, Schwartzman D, Gottlieb CD, Marchlinski FE: Repetitive monomorphic tachycardia from the left ventricular outflow tract: electrocardiographic patterns consistent with a left ventricular site of origin. *J Am Cardiol* 1997; 29: 1023–1027
 - 6) Yeh SJ, Wen MS, Wang CC, Lin FC, Wu D: Adenosine-sensitive ventricular tachycardia from the anterobasal left ventricle. *J Am Coll Cardiol* 1997; 30: 1339–1345
 - 7) Hachiya H, Aonuma K, Yamauchi Y, Harada T, Igawa M, Nogami A, Iesaka Y, Hiroe M, Marumo F: Electrocardiographic characteristics of left ventricular outflow tract tachycardia. *PACE* 2000; 23: 1930–1934
 - 8) Lerman BB, Stein K, Engelstein ED, Battleman DS, Lippman N, Bei D, Catanzaro D: Mechanism of repetitive monomorphic ventricular tachycardia. *Circulation* 1995; 92: 421–429
 - 9) Lerman BB, Stein KM, Markowitz SM: Mechanism of idiopathic left ventricular tachycardia. *J Cardiovasc Electrophysiol* 1997; 8: 571–583
 - 10) Ashikaga T, Nishizaki M, Yamawake N, Arita M, Sakurada H, Numano F, Hiraoka M: A case of ATP-sensitive idiopathic ventricular tachycardia originating from left ventricular outflow tract. *Journal of clinical cardiac electrophysiology* 1999; 22: 39–48 (in Japanese)
 - 11) Hsu J-T, Lin K-H, Luqman N, Sung RJ, Kuo C-T: Unusual features of an idiopathic ventricular tachycardia arising from the left ventricular outflow tract. *PACE* 2005; 28: 160–163
 - 12) Lerman BB, Belardinelli L: Cardiac electrophysiology of adenosine. Basic and clinical concepts. *Circulation* 1991; 83: 1499–1509
 - 13) Gupta RC, Neumann J, Durant P, Watanabe AM: A1-adenosine receptor-mediated inhibition of isoproterenol-stimulated protein phosphorylation in ventricular myocytes. Evidence against a cAMP-dependent effect. *Circ Res* 1993; 72: 65–74